

ABSTRACT

[0120] The present invention is directed to an isolated polynucleotide sequence encoding a chimeric TNF α , comprising a first nucleotide sequence encoding a domain or subdomain of a tumor necrosis factor ligand other than TNF α , wherein the encoded domain or subdomain replaces a cleavage site of native TNF α , and a second nucleotide sequence encoding a domain or subdomain of native TNF α that binds to a TNF α receptor. The encoded chimeric TNF α is significantly less susceptible to cleavage from the cellular surface and, as a result can increase the concentration of a ligand capable of binding to a TNF α receptor on the surface of a cell. The chimeric TNF α is therefore useful in methods for inducing apoptosis of a cell expressing a TNF α receptor, inducing activation of an immune system cell and treating neoplastic cells, by introducing into the cell of interest an isolated polynucleotide sequence encoding a chimeric TNF α that is expressed on the surface of the cell.